PATENT
Attorney Docket No. BNIT0003-PCT-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Søren Mouritsen et al.	Group Art Unit: 1644
Application No.: 08/955,373	Examiner: SCHWADRON, Ronald B.
Filed: October 21, 1997	
For: INDUCING ANTIBODY RESPONSE AGAINST SELF-PROTEINS WITH THE AID OF FOREIGN T-CELL EPITOPES	Confirmation No.: 7254

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION OF ALAIN DELCAYRE UNDER 37 C.F.R. § 1.132

I, Alain Delcayre, do hereby make the following declaration:

1. I received a Master's degree in Molecular and Cellular Biology/Immunology in 1984, followed by a Ph.D. in Molecular and Cellular Biology/Immunology in 1989, both from Université Pierre et Marie Curie (Paris VI) in Paris, France. I conducted my thesis research at the Institut National de la Santé et de la Recherche Médicale, Unité 23 (Laboratoire de Biochimie des Antigènes de Membrane), also in Paris.

2. Since completing my Ph.D. in 1989, I have held laboratory research positions of increasing responsibility in the biotechnology industry. My research has focused in the areas of vaccines and immunotherapy, in which I have published fifteen papers in peer-reviewed

scientific journals. I have also been listed as an inventor on eleven patent applications, several of which have issued as U.S. patents. I am currently Senior Director of Research at BN ImmunoTherapeutics, Inc. ("BNIT"), a position I have held since 2009. I have been with BNIT since 2005. A copy of my Curriculum Vita and list of publications is attached to this Declaration as Exhibit 1.

3. I have read U.S. Patent Application No. 08/955,373 ("the '373 application"), including the claims as amended, and the final Office Action issued August 4, 2010 ("Office Action"), by Examiner Schwadron. I understand that all pending claims have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In particular, I understand that the Examiner asserts that the phrase "the secondary structure of the self-protein is essentially preserved" renders claim 102 indefinite because "it is unclear what changes to the secondary structure would or would not be encompassed by the aforementioned term." Office Action, section 6, page 3.

4. I understand that a claim is definite within the statute if it sets out specific subject matter with a reasonable degree of clarity and particularity, meaning that a person of ordinary skill in the art, like myself, can understand what is claimed when reading the claim in light of the disclosure of the patent application.

5. Amended claim 102 reads:

> [a] method for inducing autoantibodies against a self-protein in a subject, said method comprising:
> administering to the subject an analog of the self-protein made by molecular biological means, wherein said analog is made by substituting one or more peptide fragments in the self-protein with a corresponding number of immunodominant foreign T-cell epitopes selected from

> ovalbumin, hen egg lysozyme, tetanus toxoid, or diphtheria toxoid T-cell epitopes,
>
> such that the secondary and tertiary structure of the self protein is essentially preserved; such that said analog induces an autoantibody response as evidenced by antibody binding to the unmodified self-protein.

6. Based on the claim language as amended, I understand that the secondary and tertiary structure of a self-protein analog is essentially preserved where: (1) the self-protein analog induces an autoantibody response in a subject; and (2) the induced autoantibodies bind to the corresponding unmodified self-protein. An immunologist of ordinary skill could easily determine whether a particular self-protein analog induces an autoantibody response in a subject, and if so, whether the induced autoantibodies bind to the corresponding unmodified self-protein using any of several common immunoassay techniques.

7. The specification as-filed confirms that understanding. As the application explains, the surprising observations underlying the claimed invention resulted from the fact that various T-cell epitopes were inserted into the self-protein, "against which it is the purpose to raise antibodies." Specification as-filed, page 3, line 28. The T-cell epitopes were substituted for fragments of the self-protein having the same number of amino acids as the introduced T-cell epitope, "thus preserving the secondary and tertiary structure of the self-protein to a large extent." *Id.*, page 3, lines 29-30. The specification further explains that "[i]t is of importance to essentially preserve the tertiary structures, as it is done in the present invention, because these structures determine the specific recognition of the non-modified self-protein by the induced [auto-]antibodies." *Id.*, page 4, lines 7-10. Thus, like the language of claim 102 as amended, the specification makes clear that the secondary and tertiary structure of the self-protein analog is essentially preserved where: (1) the self-protein analog induces an autoantibody response; and (2) the induced autoantibodies bind to the corresponding unmodified self-protein.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the '373 application or any patent issuing thereon.

Dated: November 22, 2010

By: _____
Alain Delcayre, Ph.D.